

REMARKS

I. Claim status

Applicant has amended claims 5, 8, 10-13, 21, 23, 34, and 64. Claims 2-4, 6, 9, and 14 were cancelled by earlier amendments. Upon entry of this amendment, claims 1, 5, 7, 8, 10-13, and 15-70 will be pending — claims 1, 5, 7, 8, 10-13, 19-22, and 60-70 are under examination and claims 15-18 and 23-59 are withdrawn. Claims 1 and 7 have been allowed.

All amendments are made without prejudice or disclaimer.

Support for the claim amendments can be found throughout the application, including, *e.g.*, paragraphs [0005], [0011], [0014], and [0016] of the published application, U.S. Patent Application Publication No. 20060127897, the examples, and the original claims. The amendments do not add new matter, and Applicant respectfully requests their entry.

II. Telephonic Interview

Applicant thanks Examiner Babic for conducting a telephonic interview with Applicant's representative Lawrence Shumway on April 7, 2010, to discuss the Response dated April 2, 2010, and the rejections under 35 U.S.C. § 102(b). Applicant believes the amendments and remarks submitted herein accurately reflect the content of the interview.

III. Rejections under 35 U.S.C. § 112, second paragraph

Applicant acknowledges with appreciation that the following objections and rejections have been withdrawn in the Office Action mailed April 20, 2010:

- The objection to claims 11-13, 19-22, and 60 for allegedly depending from a cancelled claim;
- The rejection of claims 8, 19-22, and 60 under 35 U.S.C. §112, ¶ 2 as allegedly indefinite for reciting “at least 8 to 2000 consecutive nucleotides of at least one nucleic acid according to claim 7”;
- The rejection of claim 8 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,474,796 to Brennan (“*Brennan*”);
- The rejection of claims 5, 8, 10, 61, and 62 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent Application Publication No. 2001/0053519 by Fodor *et al.* (“*Fodor*”).

IV. Rejection under 35 U.S.C. § 102(b)

Maintained Rejection

The Office maintains the rejection of claim 5 under 35 U.S.C. § 102(b) over *Brennan*. Office Action mailed April 20, 2010, at pp. 3-5. In response to Applicant’s arguments submitted in Reply dated April 2, 2010, the Office alleges that the claimed nucleic acid fragment “remains recited in a manner that encompass any nucleic acid fragment.” *Id.* at 4 (emphasis omitted). The Office thus suggests to amend claims 5 and 11, stating that “[a]n amendment reciting ‘The purified or isolated nucleic acid fragment...’ would obviate the instant rejection.” *Id.* at 5. With respect to claims 5 and 10-13, the Office also encourages Applicant “to amend the claim to explicitly require a specific type of amplification.” *Id.*

Applicant has amended claims 5 and 11-13 according to the Office's suggestions. Claims 5 and 11 are now directed to "The purified or isolated nucleic acid fragment," and the amended claims 5 and 11-13 recite "PCR amplification." Because claims 5 and 11-13 have been amended in the instant paper as suggested by the Examiner, Applicant respectfully requests withdrawal of the claim rejection under 35 U.S.C. § 102(b).

With respect to claims 5 and 11-13, the Office also contends that "the claimed invention does not require that the nucleic acid fragment necessarily include the sequence of both primers," suggesting an "inclusion of both primer sequences" in the claims. *Id.* at 4-5. Applicant respectfully disagrees. One of ordinary skill in the art, being familiar with PCR amplification technique, understands that the nucleic acid fragment of the instant claims necessarily includes a sequence of the recited primers or a sequence complementary to the corresponding primers. Therefore, Applicant respectfully submits that inclusion of the language related to the primer sequences, as suggested by the Office, would be redundant.

New Rejection

Claims 8, 19, 69, and 70 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by NCBI (GENBANK Accession No. U15183; 9 March 1995) ("NCBI"). According to the Office, "NCBI teaches a purified and isolated nucleic acid fragment sequence comprising 22 consecutive nucleotides of SEQ ID NO:4." *Id.* at 5. The Office alleges that "the phrase 'susceptible to be used as a probe' is not defined by the claim or specification to preclude the application of NCBI as prior art because if the sequence of NCBI was contained within a composition with a 22-mer sequence of the highlighted

sequence under appropriate hybridization conditions, it would be a matter of simple point of view or semantics as to which sequence was in fact 'probing' the other." *Id.* at 5-6.

Applicant has amended claim 8 to recite "wherein the fragment is a probe or a primer," instead of "susceptible to be used as a probe or a primer. In addition, Applicant has amended claim 8 by substituting the word "comprising" with the phrase "consisting of." Accordingly, Applicant respectfully requests that the Office withdraw this rejection of claim 8, 19, 69, and 70 under 35 U.S.C. § 102(b).

IV. Rejection under 35 U.S.C. § 103(a)

The Office has made three separate rejections under 35 U.S.C. § 103(a). First, claims 5, 8, 10-13, and 61-64 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over *Fodor*. Second, claims 5, 8, 11-13, 64, 69, and 70 are rejected as allegedly obvious over Santos *et al.*, *J. Med. Microbiol.* 39(4):298-304 (1993) ("*Santos*") in view of *NCBI*. Third, claims 21 and 60 are rejected as allegedly obvious over *NCBI* in view of U.S. Patent No. 6,221,353 to Laqueyrie *et al.* ("*Laqueyrie*").

Based on the Supreme Court's decision in *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007), the Patent Office has announced seven exemplary rationales that may support a conclusion of obviousness. (See M.P.E.P. § 2143.) All of these bases for obviousness require that one of ordinary skill in the art, without knowing anything of the claimed invention, would not only be motivated to produce that invention, but also would have a reasonable expectation of success and achieve predictable results. For the reasons outlined below, Applicant respectfully submits that the Office has failed to

establish a *prima facie* case of obviousness over *Fodor*, over the combination of *Santos* and *NCBI*, and over the combination of *NCBI* and *Laqueyrie*.

Fodor

The Office rejects claims 5, 8, 10-13, and 61-64 under 35 U.S.C. § 103(a) as allegedly obvious over *Fodor*. Specifically, the Office contends that “*Fodor* teaches an ‘n-mer’ array comprising every permutation of a 10-mer oligonucleotide,” and that the reference “further suggests the production of solid supports comprising a set of every permutation (4ⁿ) of different length oligonucleotides or n-mers in a range from 2-25-mers.” Office Action at 7-8. The Office thus concludes that “a product comprising a purified or isolated oligonucleotide of 20 contiguous nucleotides of SEQ ID NO:4 (claims 8 and 11-13), or SEQ ID NOs: 13-18 (claims 5, 10, and 61-64) would have been *prima facie* obvious to a person of ordinary skill in the art.” *Id.* at 8. Applicant respectfully disagrees.

This rejection is apparently based on alleged inherent disclosure of the claimed nucleotide sequences by *Fodor*’s report of oligonucleotide arrays involving all possible 2-mers, 10-mers, or 25-mers. It is well established that “[o]bviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established.” M.P.E.P. § 2141.02, citing *In re Rijckaert*, 9 F.2d 1531 (Fed. Cir. 1993). Indeed, “[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.” *Rijckaert*, 9 F.2d at 1534 (emphasis added). The Federal Circuit and its predecessor court have long noted that “inherency is quite immaterial if . . . one of ordinary skill in the art would not

appreciate or recognize that inherent result.” *In re Naylor*, 152 U.S.P.Q. 106, 108 (C.C.P.A. 1966).

Fodor does not render the instant claims obvious because it neither teaches nor suggests any of the claimed nucleotide sequences. In fact, the reference simply describes n-mer arrays that use oligonucleotides of a specific length (2, 10, or 25 nucleotides) but of any possible sequence. *Fodor* itself discloses that a 10-mer array, for example, comprises 1,048,576 possible sequences. *Fodor* at [0101]. The teachings of this reference thus would not have led one skilled in the art to predict, with a reasonable expectation of success, any specific sequence relevant to the instant claims out of the tremendous number of possible nucleotide combinations. For example, nothing in *Fodor* teaches or even remotely suggests a fragment of SEQ ID NO:1 or 4, at least 12 nucleotides in length (e.g., claim 8), at least 15 nucleotides (e.g., claim 64), or the specific 20-mers of SEQ ID NOs:13-18 (e.g., claims 5, 10-13, and 61-63). Even less predictable are the recited pairs of 20-mers (e.g., claims 5, 11-13, 62, and 63) or nucleic acid fragments amplified from *Mycobacterium* complex using such 20-nucleotide primers (e.g., claims 5, 11-13). Thus, the Office has failed to establish a *prima facie* case of obviousness.

Furthermore, as explained above, the nucleic acid fragments of claims 5 and 11-13 include a sequence of the recited pairs of 20-nucleotide-long primers, or a complementary sequence, and the fragments are therefore at least 40 nucleotides in length. *Fodor* does not teach or suggest sequences that are longer than 25-mers and thus does not render these claims *prima facie* obvious.

For at least these reasons, Applicant submits that claims 5, 8, 10-13, and 61-64 are patentable over *Fodor*. Accordingly, Applicant respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 103(a).

Santos* In View of *NCBI

Claims 5, 8, 11-13, 64, 69, and 70 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over *Santos* in view of *NCBI*. Specifically, the Office asserts that “*Santos* teaches designing a probe sequence to the *Mycobacterium leprae* genome.” Office Action at 9. The Office acknowledges that the reference “does not specifically teach a sequence recited in claims 5, 8, or 11,” but proceeds to argue that the “*M. leprae* genome sequence, the sequence from which the *Santos* oligonucleotide was derived, is a sequence that was well known at the time of invention,” and “[t]hus, the binding site of a claimed oligonucleotide, a 22-mer for example, is suggested within the sequence disclosed by [*NCBI*].” *Id.* The Office concludes that “since the claimed sequences simply represent structural homologs of those sequences disclosed in the prior art, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds, the claimed 22-mer sequence within NCBI U15183 is *prima facie* obvious over the cited references.” *Id.* at 10. Applicant respectfully disagrees.

First, Applicant points out that both *Santos* and *NCBI* are related to nucleotide sequences of *M. leprae*, and not SEQ ID NO:1 or SEQ ID NO:4. In this rejection, the Office merely seems to allege that, because the *NCBI* sequence and the claimed sequences are structurally similar, one skilled in the art would have been motivated to try to design the claimed nucleotide sequences based on NCBI’s disclosure of the *M. leprae* cosmid. However, the Office has not shown that one skilled in the art would

have predicted, based on the teachings of *Santos* and *NCBI*, which specific oligonucleotide sequence within the 36,800-nucleotide sequence of the *M. leprae* cosmid could be used as a probe or a primer specific for SEQ ID NO:1 or SEQ ID NO:4. Thus, the Office has failed to establish a *prima facie* case of obviousness.

Furthermore, as argued above, the claimed nucleic acid fragments of claims 5 and 11-13 include a sequence of the recited pairs of 20-nucleotide-long primers, or a complementary sequence, and the fragments are therefore at least 40 nucleotides in length. The at least 18-nucleotide difference between the 22-mer sequence of *NCBI* and the claimed fragments would present one skilled in the art with more than 4¹⁸ possible sequences. Therefore, the claimed fragments would not have been obvious to try, and they are not *prima facie* obvious over the cited references.

For at least these reasons, Applicant submits that claims 5, 8, 11-13, 64, 69, and 70 are patentable over *Santos* and *NCBI*. Accordingly, Applicant respectfully requests that the Office withdraw this rejection under 35 U.S.C. § 103(a).

NCBI In View of Laqueyrie

Claims 21 and 60 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over *NCBI* in view of *Laqueyrie*. Specifically, the Office asserts that “*Laqueyrie* teaches the production of recombinant cells comprising cosmids for the study of such cosmids,” and that “it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to incorporate the *NCBI* cosmid into an *E. coli* cell for example since *Laqueyrie* suggests such a product to produce copies of target cosmid sequences for further study.” Office Action at 10-11. Applicant respectfully traverses.

Claims 21 and 60 are directed to a recombinant cell “comprising a nucleic acid sequence selected among nucleic acids according to any of claims 1, 5, 7, 8, 11, 12, 13, and 64.” For the reasons outlined above, the nucleotide sequences recited in these claims are novel and non-obvious over the cited prior art. Claims 21 and 60 are, therefore, also patentable over *NCBI* and *Laqueyrie*. Accordingly, Applicant respectfully requests that the Office withdraw this its under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims. The Examiner is encouraged to contact the undersigned with any questions to facilitate prosecution.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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